FDA Alert for Healthcare Professionals

Vardenafil (marketed as Levitra)

FDA ALERT [07/2005]: FDA has approved new labeling for Levitra, Viagra, and Cialis regarding postmarketing reports of vision loss related to NAION (non-arteritic anterior ischemic optic neuropathy). Most, but not all, of these patients had underlying anatomic or vascular risk factors for development of NAION, including: low cup to disc ratio ("crowded disc"), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia and smoking. Given the small number of events, the large number of users of PDE-5 inhibitors and the fact that this event occurs in a similar population to those who do not take these medicines, it is not possible to determine whether these events are related directly to the use of PDE-5 inhibitors, to the patient's underlying vascular risk factors or anatomical defects, to a combination of these factors, or other factors. We cannot currently draw a conclusion of cause and effect. FDA will continue to evaluate the issue.

This information reflects FDA's current analysis of data available to FDA concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of Levitra, please contact the FDA MedWatch program at 1-800-FDA-1088 or http://www.fda.gov/medwatch/report/hcp.htm

Recommendations

Physicians should:

- advise patients to stop use of all PDE-5 inhibitors and seek medical attention in the event of a sudden loss of vision in one or both eyes. Such an event may be a sign of non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision, which can result in permanent loss of vision.
- discuss with patients the increased risk of NAION in individuals who have already experienced NAION in one eye, including whether such individuals could be adversely affected by use of vasodilators such as PDE-5 inhibitors.

Data Summary

As of May 18, 2005, a total of 43 cases of ischemic optic neuropathy (ION) among patients using the marketed PDE-5 inhibitors (sildenafil, tadalafil, vardenafil) have been reported to the FDA's Adverse Event Reporting System. Since approval, 38 cases have been identified in association with sildenafil, 4 cases have been identified in association with tadalafil and one case has been identified in association with vardenafil. Most of these cases (25/43) appear to be the non-arteritic anterior ischemic optic neuropathy (NAION) subtype. Thirty-six of the 43 cases reported accompanying visual loss, and 26 of these 36 cases reported the visual loss as continuing or permanent. Most of the patients in these cases reported vascular risk factors for NAION that overlap with vascular risk factors for erectile dysfunction (such as age over 50, low cup to disc ratio, hypertension, diabetes, smoking, etc), making direct attribution to PDE-5 inhibitors not possible. However, the clinical attributes of some of the cases (e.g., a temporal relationship in 19 sildenafil cases, 4 tadalafil cases, and the one vardenafil case, and the report of

recurrent ocular symptoms that might reflect NAION in five sildenafil cases and one tadalafil case), raise concern in regard to the role of PDE-5 inhibitors.

One case associated with vardenafil use was reported to FDA in 2004. A male patient in his mid-50s with no documented hypertension, diabetes and hyperlipidemia took 10mg vardenafil for the first time and experienced vision loss in his left eye the next morning. The patient lost central vision in his left eye, reportedly due to transient ischemia. It is unknown if the vision loss reversed or persisted.

FDA is aware of 6 additional cases of vision loss following vardenafil administration, reported as serious adverse events in the Bayer Global Drug Safety Database.